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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,745	06/27/2003	Peter Gluckman	704652-9001	5345

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,745	GLUCKMAN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *78,79 and 81-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *78,79 and 81-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/185,804.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The maintenance fees due at 3.5 years, 7.5 years, and 11.5 years after the issue date of U.S. Patent No. 5,714,460 have been paid, and therefore the reissue procedures are available for this patent.

This reissue application was originally filed within two months of the mailing date of the final judgment of interference 104,553, and therefore the reissue procedures are available for this patent.

2. This application is objected to under 37 CFR 1.172(a) as the assignee has not established its ownership interest in the patent for which reissue is being requested. An assignee must establish its ownership interest *in order to support the consent to a reissue application required by 37 CFR 1.17*2(a). The submission establishing the ownership interest of the assignee is informal. There is no indication of record that the party who signed the submission is an appropriate party to sign on behalf of the assignee. 37 CFR 3.73(b).

A proper submission establishing ownership interest in the patent, pursuant to 37 CFR 1.172(a), is required in response to this action.

Papers attempting to establish the consent of assignee to the reissue were filed on November 1, 2004. However, the papers are contradictory. One paper, signed by Timothy R. Schwartz, PhD., states that Genentech, Inc. is the owner of the entire right, title and interest in and to U.S. Patent No. 5,714,460. A second paper, signed by Paulina Lucrynska (sp.?), states that NeuronZ Limited is the owner of the entire right, title and interest in and to U.S. Patent No. 5,714,460. Two separate legal entities cannot each be the owner of the entire right, title and interest in a single U.S. patent. Further, according to the assignment records of the U.S. Patent

and Trademark Office, NeuronZ LTD is the only assignee of record for U.S. Patent No. 5,714,460. Correction is required.

In their Remarks filed May 12, 2010, Applicants explain how at the time the above consents were signed, the two inventors had assigned their rights to separate entities, i.e. to Genentech, Inc. and to Auckland Uniservices Ltd. It should be noted that neither of the consents filed in this application is signed by Auckland Uniservices Ltd. Applicants also explain how each inventor, being a joint owner of the patent, owns an undivided 100% interest in the patent, and cite to 35 U.S.C. 262 and MPEP 301. However, as set forth in MPEP 301(IV), second paragraph, "Multiple parties may **together** own the entire right, title and interest of the patent property" (emphasis in original); and in the third paragraph, "Each individual inventor may only assign the interest he or she holds; thus, assignment by one joint inventor renders the assignee a partial assignee." The two consents filed November 1, 2004 make no mention of other assignees/owners of the patent property. Each consent indicates that each assignee individually owns the entire right, title and interest of the patent, so that each consent contradicts the other with respect to ownership of the patent and each is inconsistent with the fact pattern presented in the Remarks.

3. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,583,114 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

4. The disclosure is objected to because of the following informalities: In the amended paragraph at column 1, lines 3-8, second-to-last sentence, the recitation that priority to U.S. Patent Application Serial No. 08/460,365 is claimed under 35 U.S.C. 120 is incorrect. This application can not claim priority under 35 U.S.C. 120 based upon application serial no. 08/460,365 because the two applications were never copending, i.e. this reissue application was not filed before the patenting of the '365 application. See 35 U.S.C. 120, first sentence, and MPEP 201.11(II)(B). By the terms of the statutes, a reissue application filed under 35 U.S.C. 251 is incapable of claiming priority under 35 U.S.C. 120 to the application from which issued the patent forming the basis for the reissue application. (Incidentally, the first paragraph of the specification also does not recite a relationship, i.e. continuation, divisional, or continuation-in-part, between this application and the '365 application, which is another requirement for a claim for priority under 35 U.S.C. 120. See MPEP 201.11(III)(A).) Appropriate correction is required.

5. In any future claim listing filed in this application, the underlining below the status identifier "[Canceled]" for claim 80 should be removed.

6. The reissue oath/declaration filed October 3, 2006 is defective (see 37 CFR 1.175 and MPEP § 1414) because of the following:

The declaration lacks an acceptable duty to disclose statement. Note that the declaration refers only to a duty to disclose as defined by 37 CFR 1.56(a). However, 37 CFR 1.175(a) requires a reissue oath or declaration to comply with the requirements of § 1.63, and § 1.63(b)(3) defines the duty to disclose by reference to all of 37 CFR 1.56. See also MPEP 1414(IV)(C).

Claims 78, 79, and 81-96 are rejected as being based upon a defective reissue declaration under 35 U.S.C. 251. See 37 CFR 1.175. The nature of the defect is set forth above.

Forms PTO/SB/51 and PTO/SB/52 are available to help avoid errors like the one indicated above.

7. Claims 78, 79, and 81-92 are rejected under 35 U.S.C. 251 as being broadened in a reissue application filed outside the two year statutory period. In particular, the patent claims require the mammal to have actually suffered neural damage. However, the instant claims only require the mammal to be "suspected" of suffering from cerebral ischemia. Because a mammal can be suspected of suffering from cerebral ischemia without actually suffering from cerebral ischemia, e.g., because of the result of a faulty diagnosis or because of the result of a preliminary diagnosis based upon insufficient information, the instant claims embrace the treatment of mammals not embraced by the patent claims, i.e. of mammals suspected of but not actually suffering from cerebral ischemia. A claim is broader in scope than the original claims if it contains within its scope any conceivable product or process which would not have infringed the original patent. A claim is broadened if it is broader in any one respect even though it may be narrower in other respects.

8. Claims 78, 79, and 81-92 are rejected under 35 U.S.C. 251 as being based upon new matter added to the patent for which reissue is sought. The added material which is not

supported by the prior patent is as follows: The step of identifying a mammal suspected of suffering from cerebral ischemia in new claim 78 is new matter. The original patent does not recite an identifying step and does not recite mammals which are "suspected" of suffering from cerebral ischemia. In the original patent, including column 1, lines 20-60, and column 8, line 65 - column 13, line 45, cited by Applicants as support for the new claim language, there is no identifying step because all mammals discussed therein are known to have suffered central nervous system damage. In the original patent, the mammals are not "suspected" of suffering from cerebral ischemia because all mammals discussed therein are known to have suffered central nervous system damage. The recitation of intrathecal and epidural administration, or of administration by the cerebral vasculature or via the carotid artery, in new claims 82, 83, 85, and 86 is new matter. The patent does not recite such methods of administration. The recitation of ischemia caused by embolism, thromboembolism, and toxin in new claims 90-92 is new matter. The patent does not disclose these particular types of cerebral ischemia.

9. Claims 78, 79, and 81-92 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. That subject matter identified as constituting new matter under 35 U.S.C. 251 for the reasons set forth in section 8 above also lacks written description in the original disclosure of the invention, for the same reasons.

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 78, 79, and 81-92 are rejected under 35 U.S.C. 103 as being estopped on the merits by final judgment in Interference No. 104,533. See also 37 CFR 41.127(a) and MPEP 2308.03, Examples 2 and 3 (Rev. 4, October 2005). In the section of the interference count which corresponds to claim 1 of U.S. Patent No. 5,714,460, a mammal suffering from neural damage after a CNS insult is treated with IGF-1 or a biologically active analogue thereof. Claim 3 of the '460 patent, which specifies that CNS insult is ischemic injury, was designated as corresponding to the count. While Applicants moved to designate claim 3 as not corresponding to the count, this motion was denied. See the Decision On Motions, pages 27-29. Thus, the subject matter of claim 3 of the '460 patent has already been held to be patentably indistinct from the count, and this denial provides basis for this determination of interference estoppel. Instant claim 78 differs from claim 3 of the '460 patent in that instant claim 78 does not require the mammal to actually be suffering from cerebral ischemia, but rather only requires the mammal to be suspected of suffering from cerebral ischemia. In this respect, instant claim 78 is broader in scope than claim 3 of the '460 patent, and does not patentably distinguish over the subject matter lost to Applicants in the Interference proceeding. Instant claim 78 also differs from claim 3 of the '460 patent in that instant claim 78 specifies the result of a reduced loss of neurons and/or infarction associated with cerebral ischemia without significantly altering the brain temperature of the mammal being treated. These results are not specified in claim 3 of the '460 patent. However, instant claim 78 and claim 3 of the '460 patent recite the same method steps using the same compounds directed to the same patients. Because the method steps, compounds, and patients are the same, inherently the method of claim 3 of the '460 patent must produce the same results recited in instant claim 78, and therefore instant claim 78 does not patentably distinguish

over claim 3 of the '460 patent. Applicants have not provided any evidence that a significant alteration of brain temperature might be expected upon administration of IGF-1 and/or an analogue thereof, nor have they disclosed any special administration steps which are relied upon in order to avoid a significant alteration of brain temperature. A prior art reference (i.e. the lost count or the subject matter of the claims lost in interference) need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See, e.g., In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002). With respect to instant claims 79 and 84, claims 14 and 15 of the '460 patent recite specific types of administration via the cerebrospinal fluid. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460 patent by administering the IGF-1 or analogue thereof into the cerebro ventricle or into the lateral ventricle of the brain of the mammal being treated as is also claimed by the '460 patent. See also the Decision On Motions, page 28, lines 9-14. With respect to instant claim 81, the interference count and Applicants' claims lost in interference do not recite treating a mammal who is a human. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat a mammal who is human in the method of claim 3 of the '460 patent, because treatment of humans is generically encompassed by the mammals recited in claim 3 of the '460 patent, because one skilled in the art is most motivated to treat ischemia in humans compared to all other mammals, and because there is no evidence that treatment of ischemia using IGF-1 or analogues thereof is significantly different for humans than for other mammals. With respect to instant claims 82, 83, 85, and 86, the interference count and Applicants' claims lost in interference do not recite intrathecal or epidural administration, and do

not recite administration via the cerebral vasculature or via the carotid artery. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the IGF-1 or analogues thereof in claim 3 of the '460 patent intrathecally, epidurally, via the cerebral vasculature, or via the carotid artery, because these are known methods of administering drugs to the CNS whereby the BBB is avoided. With respect to instant claims 88 and 89, claim 3 of the '460 patent recites treatment of ischemic injury, claim 4 of the '460 patent recites treatment of traumatic injury, and claim 2 of the '460 patent recites treatment of hypoxic injury. However, the interference count and Applicants' claims lost in interference do not recite treating ischemic injury caused by traumatic injury, and do not recite treating ischemic injury caused by hypoxic injury. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460 patent when caused by traumatic injury or by hypoxic injury, because treatment of all three types of injuries is claimed by the '460 patent and their treatment was designated as corresponding to the interference count, and because designation of these injuries as a cause or effect would not have been expected to affect the ability of these injuries to be treated in accordance with claims 2-4 of the '460 patent. With respect to instant claims 87 and 90-92, the interference count and Applicants' claims lost in interference do not recite these particular causes of ischemic injury. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat ischemic injury according to claim 3 of the '460 patent where the ischemic injury is caused by asphyxia, embolism, thromboembolism, or a toxin, because these are known causes of ischemic injury, because claim 3 of the '460 patent embraces the treatment of ischemic injury

regardless of its cause, and because it would be desirable to treat neural damage affecting glia or other non-cholingeric cells regardless of the particular cause of the neural damage.

In the paper titled "Notice Under 37 C.F.R. §1.178(b)" filed June 27, 2003, Applicants refer to footnote 17 of the Decision On Motions in the interference as indicating that Applicants would not be estopped from pursuing in a reissue application narrower claims that would not have been obvious in view of the lost count. However, the basis for this approach is that the reissue claims must be nonobvious over the lost count. As indicated above, current reissue claims 78, 79, and 81-92 remain obvious over the lost count and/or are not patentably distinct from the subject matter of the lost claims. Alternatively, the current reissue claims are obvious over the subject matter previously held to be unpatentable to Applicants under 35 U.S.C. 102(g)(1).

12. Claims 78, 79, and 81 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 90/14838. The WO Patent Application '838 teaches treating stroke, i.e. ischemia, in mammals, including humans, by administering IGF-I or a functional derivative thereof, or by administering IGF-II or a functional derivative thereof. The treatment enhances the survival of neuronal cells which are at risk of dying as a result of the stroke. The active agents are administered parenterally, including intracranially and intraspinally. See, e.g., the Abstract; page 6, lines 18-28; page 12, lines 1-13; page 20, lines 29-35; page 21, lines 1-11, and claim 77. IGF-I functional derivatives, IGF-II, and IGF-II functional derivatives are biologically active analogs of IGF-I. Because the same active agents are being administered to the same mammals according to the same method steps in order to treat the same CNS injuries, inherently the brain temperature of the mammals being treated will not be significantly altered in the

method of the WO Patent Application '838 to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the WO Patent Application '838 and Applicants claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of the WO Patent Application '838.

With respect to the inherency rejection, note that a prior art reference need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See Ex parte Novitski, 26 USPQ2d 1389, 1391 (POBA 1993); In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002); and more generally MPEP 2112.

See also the Decision On Motions, pages 39-43, in which it was held that all claims of the '460 patent which corresponded to the count were unpatentable over the prior art.

13. Claims 82-92 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 90/14838. Application of the WO Patent Application '838 is the same as in the above rejection of claims 78, 79, and 81. The WO Patent Application '838 does not teach the particular administration methods recited in claims 82-86. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the active agents of the WO Patent Application '838 by the administration methods recited in instant claims 82-86, because the WO Patent Application '838 is not limited to any particular method of administration (see page 21, lines 1-7), and because the administration methods recited in instant claims 82-86 are known methods of administering drugs to the CNS whereby the BBB is avoided. The WO Patent Application '838 does not teach treating stroke caused by the particular conditions recited in claims 87-92. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to treat according to the WO Patent Application '838

stroke caused by the particular conditions recited in instant claims 87-92, because the WO Patent Application '838 is not limited to the treatment of stroke caused by any particular condition, because the particular conditions recited in instant claims 87-92 are known causes of stroke, and because it would be desirable to enhance the survival of neuronal cells at risk of dying due to the stroke regardless of the particular cause of the stroke.

14. Claims 78, 79, 84, and 89 are rejected under 35 U.S.C. 102(a) as being anticipated by the Gluckman et al article (Biochem. Biophys. Res. Comm. vol. 182, pages 593-599). The Gluckman et al article teaches subjecting rats to inhalational hypoxia, resulting in hypoxic-ischemic injury, and then administering IGF-1 by cerebroventricular injection to the injured hemisphere. Neuronal loss is reduced, especially in the lateral cortex and in the dentate gyrus. See, e.g., the Abstract and page 595, first full and last paragraphs. Because the same active agent is being administered to the same mammal according to the same method steps in order to treat the same CNS injury, inherently the brain temperature of the mammal being treated will not be significantly altered in the method of the Gluckman et al article to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the method of the Gluckman et al article and Applicants claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of the Gluckman et al article.

With respect to the inherency rejection, note that a prior art reference need not recognize or suggest Applicants' intended results in order to anticipate Applicants' claimed method on the basis of inherency. See Ex parte Novitski, 26 USPQ2d 1389, 1391 (POBA 1993); In re Cruciferous Sprout Litigation, 64 USPQ2d 1202 (CAFC 2002); and more generally MPEP 2112.

15. Applicant's arguments filed May 12, 2010 have been fully considered but they are not persuasive.

Applicants did not traverse or otherwise respond to the rejection under 35 U.S.C. 251 based upon a defective reissue declaration.

The rejection under 35 U.S.C. 251 based upon the presence of broadened claims in a reissue application filed outside the two year statutory period is maintained with respect to the recitation of mammals "suspected" of suffering from cerebral ischemia. Applicants contend that pending claims must be given their broadest reasonable interpretation consistent with the specification. The examiner agrees. However, the corollary to this rule of interpretation is that limitations found only in the specification will not be read into the claims, especially during ex parte prosecution when it is possible for Applicants to amend the claims in order to resolve issues of claim scope. See MPEP 2111.01. Further, it is not per se unreasonable to interpret claim limitations literally, and to bestow upon non-technical words their ordinary and customary meaning. Accordingly, a mammal "suspected" of suffering from cerebral ischemia need not actually be suffering from cerebral ischemia. This genus of mammals to be treated is broader than the genus of mammals to be treated in the patent claims, which require the presence of neural damage suffered after a CNS insult affecting glia or other non-cholinergic cells. If Applicants do not wish their reissue claims to be interpreted as covering treatment of mammals that are not suffering from cerebral ischemia, all they have to do is to delete "suspected of" from claim 78, and the claim will explicitly be limited to the coverage sought in Applicants' Remarks. Applicants contend that adding an identification step (compared to the patent claims, which lack an identification step) necessarily narrows the scope of the subject matter being claimed.

However, Applicants have not merely added an identification step, but have replaced a patented claim limitation, requiring a mammal which has suffered neural damage due to CNS insult affecting glia or other non-cholinergic cells, with a new and broader claim limitation requiring the mammal only to be "suspected" of suffering from cerebral ischemia.

The new matter rejection under 35 U.S.C. 251, and the corresponding rejection under 35 U.S.C. 112, first paragraph, are maintained with respect to the identifying step recited in instant claim 78. Applicants cite to column 1, lines 20-60, of the patent as support for the identifying step recited in instant claim 78. However, this section of the patent disclosure does not contain any discussion of an identifying step. The examiner agrees that the specification discloses and clearly contemplates treating mammalian patients suffering from cerebral ischemia. This aspect of the claimed invention is not considered to be new matter. However, the examiner maintains that the specification does not disclose or contemplate identifying mammals which might be suffering from cerebral ischemia and treating the entire genus of such mammals. Applicants again make reference to the rule that claims are to be given their broadest reasonable construction consistent with the specification. However, this rule of claim interpretation does not serve to limit claims so as to overcome a new matter rejection. Further, as noted above, it is reasonable to interpret the claims as reciting an identifying step and as embracing the treatment of mammals who are suspected of but do not actually suffer from cerebral ischemia. The rule of claim interpretation does not provide a basis for arguing that explicitly recited claim limitations are necessarily supported by the disclosure of the invention.

Applicants cite to column 5, lines 45-50 and 43-46, as support for the particular methods of administration recited in instant claims 82, 83, 85, and 86. However, the generic disclosure in

these sections of the specification does not provide support for intrathecal and epidural administration in particular or for administration via the cerebral vasculature or the carotid artery in particular. While one of ordinary skill in the art might consider these administration methods to be well-known or obvious administration methods, the new matter/written description issue concerns whether Applicants contemplated these particular administration methods and disclosed them as part of their invention. These particular administration methods are not expressly, implicitly, or inherently disclosed in the specification.

Applicants cite to column 1, lines 44-61, as support for the particular causes of cerebral ischemia recited in instant claims 90-92. However, embolism and thromboembolism are not mentioned in the cited section of the specification or anywhere else in the disclosure. While CNS damage by toxin is disclosed at column 1, lines 37-38, and at column 13, lines 28-29, toxins are listed separately from ischemia as a cause of CNS damage, and toxins are not listed as a cause of cerebral ischemia.

The new matter rejection under 35 U.S.C. 251, and the corresponding rejection under 35 U.S.C. 112, first paragraph, with respect to the particular causes of cerebral ischemia recited in instant claims 87 and 88, are withdrawn. Support for these particular causes is found especially at column 1, lines 48-50 and 61, and at column 6, lines 33-35.

The interference estoppel rejection and the prior art rejections set forth in sections 11-14 of the Office action mailed November 12, 2009 are maintained and repeated above. Applicants contend that it is unexpected that IGF-1 can prevent damage associated with ischemia when injected in volumes which do not alter brain temperatures, and that this result is not inherent in the high volume doses taught in the prior art. However, the examiner is unable to find any

disclosure in the patent of a relationship between injection volume and brain temperature of the mammal being treated. The claims also do not contain any explicit limitation as to the injection volume of the IGF-1. Applicants' argument that the prior art teaches high volume doses is not supported by any citations or evidence that the prior art injection volumes are actually high; and in any event, in the absence of a volume limitation in Applicants' claims, the prior art can not be distinguished on the basis of injection volume. Finally, Applicants have not submitted any evidence that in the methods of the closest prior art of record, brain temperatures are significantly altered. In order to rebut the prima facie cases of anticipation and rejection on the basis of unexpected results, Applicants must demonstrate that the claimed invention achieves a result not actually achieved by the prior art methods. Comparative evidence between Applicants' claimed method and the prior art methods is currently lacking.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
May 21, 2010